Association of a regulatory anti-oxidant and drug-metabolising gene with multi-morbidity and adverse drug reactions in older adults

[1,2]G Scutt, [1]A Overall, [1]P Bakrania, [3]E Krasteva, [4]N Parekh, [4]K Ali, [5]G Davies, [4]C Rajkumar

1. School of Pharmacy and Biomolecular Sciences, University of Brighton, Brighton, UK
2. Pharmacy department, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK
3. Department of Geriatric Medicine, Dartford and Gravesham NHS Trust, Dartford, UK
4. Department of Geriatric Medicine, Brighton and Sussex Medical School, Brighton, UK
5. Institute of Pharmaceutical Science, King's College London, London, UK

Introduction Multimorbidity and adverse drug reactions (ADR) are problems associated with ageing populations. Exploring underlying genetic predispositions might help to risk-stratify patients for early intervention. The nuclear factor erythroid 2-like 2 (Nrf2) protein regulates antioxidant and de-toxifying effectors in the cell. Nrf2 expression declines with age, potentially increasing vulnerability to multimorbidity and ADR. We hypothesise that single nucleotide polymorphisms (SNPs) at 3 loci in the Nrf2 gene are associated with multimorbidity and ADR in older adults.
Methods One-hundred and twenty-seven patients were recruited from a sub-population of the PRIME study (a multicentre prospective cohort study that followed older adults over 8-weeks post-discharge to determine ADR status). Donated genetic material was sequenced to determine genotype at 3 loci: rs6721961, rs35652124 and rs6706649 and then analysed for association with ADR (Naranjo Algorithm), multimorbidity (≥3 conditions defined by the Charlson Index (CI)).
Results One-hundred and twelve patients (mean age 76.6±7.3 years, 55.4% female) were successfully genotyped. In patients aged 65-79, those with the rs35652124 A allele showed increased odds of having ≥3 co-morbidities (OR 9.03 95%CI 1.16-70.2, p=0.0127). Individuals with the CGG haplotype in this age-group showed reduced odds of multimorbidity (OR 0.11, 95% CI 0.01-0.86, p=0.001). No association between Nrf2 geno/haplotype and ADR was identified.
Conclusions Polymorphisms in the Nrf2 gene are associated with multimorbidity, but not ADR, in older adults.